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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/713,432	11/13/2003	Bruce N. Ames	B00-001-3	9626

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RICHARD ARON OSMAN
SCIENCE AND TECHNOLOGY LAW GROUP
242 AVE VISTA DEL OCEANO
SAN CLEMENTE, CA 92672

EXAMINER

JONES, DWAYNE C

ART UNIT	PAPER NUMBER
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1614

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/713,432

Applicant(s)

AMES ET AL.

Examiner

Dwayne C Jones

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-57 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-57 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>11/13/03</u> . | 6) <input type="checkbox"/> Other: ____. |

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DETAILED ACTION

Status of Claims

1. Claims 1-57 are pending.
2. Claims 1-57 are rejected.

Information Disclosure Statement

3. The information disclosure statement filed November 13, 2003 has been reviewed and considered, see enclosed copy of PTO FORM 1449.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 4, 5, 7, 9-29, 31, 32, 39-44, 51-53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
6. Claims 4, 5, 7, 9-29, 31, 32, 39-44, 51-53 recite the limitation "C1-C18" compounds over ten carbon atoms, such as "N-(n-dodecyl)hydroxylamine", "N-(n-decahexyl)hydroxylamine", "N-(n-decaoctyl)hydroxylamine", "anthryl", "phenanthryl" for instance in claims 5 and 7 respectively. There is insufficient antecedent basis for this limitation in the claim. Moreover, any compound that possesses more than ten carbon atoms, as defined by claim 4, and depends from claim 4 does not have antecedent basis for these compounds.

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7. Claims 4, 7, 10, 13, 16, 19, 22, 25, 28, 31, 34, 37, 40, 43, 46, 49, and 52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claims 4, 7, 10, 13, 16, 19, 22, 25, 28, 31, 34, 37, 40, 43, 46, 49, and 52 recite the limitation "R" in each of these claims. There is insufficient antecedent basis for this limitation in the claim because there is claim dependency on claim 4.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

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the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Krishna et al. is maintained and repeated for both the above-stated and reasons of record. Krishna et al. teach of the protective effects of inter alia hydroxylamines. Krishna et al. teach that cellular damage may result from the cytotoxicity of reactive oxygen species, (see column 1, page 3477). Krishna et al. also teach that the reactive oxygen species are byproducts of normal processes in aerobic environments, and when there are imbalances in these reactive oxygen species oxidative stress results to cells, (see page 3477). Krishna et al. also disclose that hydroxylamines have been shown to protect mammalian cells exposed to reactive oxygen species, such as super oxide, hydrogen peroxide, organic hydroperoxides, and redox cycling and anticancer agents, (see column 2, page 3478). In addition, Krishna et al. teach of screening methods to test the effectiveness of hydroxylamines to provide protection to mammalian cells that are exposed to a reactive oxygen species, namely hydrogen peroxide. The results were performed with an in vitro assay, (see column 2, page 3478). In the assay model of this teaching the efficacy of the antioxidant, such as hydroxylamine, was evaluated by exposing the cells to a reactive oxygen species, namely hydrogen peroxide, and

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assessing the viability of the cells both in the absence and in the presence of a fixed concentration of the test compound, (see column 2, page 3480). The assessment would compare the amounts of the reactive oxygen species present, while the instant invention is comparing the amounts of the antioxidant of the hydroxylamine present after contact with the cells. There are many ways to measure the concentration of an assay, such as a decrease in the concentration of the unwanted species or compound, (as in Krishna et al.) or still by measuring the concentration of the antioxidant compound of the hydroxylamine (as is obviously claimed by applicant).

13. The instant claims differ only in screening methods for primary hydroxylamines whereas the prior art reference of Krishna et al. are directed to screening methods with the utilization of secondary amines. The skilled artisan would most certainly been motivated from the screening methods of Krishna et al. to employ other antioxidant or cytoprotective hydroxylamine compounds to protect cells from the deleterious effects due to oxidative damage due to inter alia, reactive oxygen species. The generation of reactive oxygen species, as taught by Krishna et al., is evident in many various biochemical and aerobic environments. Accordingly, if a cellular event such as from a variety of scenarios, for instance ischemia or inflammation or cancer or cytokines or still other events, which can generate and cause oxidative damage to a cell, would be obviously protected with the presence of hydroxylamine compounds, as clearly taught by Krishna et al. Clearly, it would have been obvious to the skilled artisan to utilize other hydroxylamine compounds and derivatives, which would obviously include primary hydroxylamine compounds and their derivatives, because the reaction between the

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oxidative damage lies between the reactive oxygen species and they hydroxylamine moiety. The skilled artisan would additionally be motivated to use primary hydroxylamine compounds and their derivatives especially since the hydroxylamine moiety of a primary hydroxyl amine is less sterically hindered than a primary hydroxylamine compound. In addition, one having ordinary skill in the art would have been motivated to use primary N-hydroxylamines to offset the deleterious effects of reactive oxygen species to cells when the prior art specifically teaches that secondary N-hydroxylamines also perform this very same function. For this reason, the skilled artisan would expect that compounds with primary N-hydroxylamines would also reduce the effects of reactive oxygen species to cells because the only structural difference lies with the presence of absence of a hydrogen atom attached to the functional group of the N-hydroxylamine moiety. Moreover, the skilled artisan would even expect that the structurally-related compounds of primary N-hydroxylamines would react more readily than the secondary N-hydroxylamines due to the absence of a secondary carbon-containing moiety, thus decreasing the steric hinderence of the secondary N-hydroxylamine. The amount and level of skill involved with substituting "bulky" groups, such as alkyl moieties for less "bulky" groups, such as a hydrogen atom, is well within the level of the skilled artisan. In fact, the replacement of an alkyl group for a hydrogen atom is expected and obvious, rather than as purported by applicants as unexpected and nonobvious because of the difference in steric hinderence between a primary N-hydroxylamine and a secondary N-hydroxylamine. Furthermore, one having ordinary skill in the art would have been motivated to use closely-related N-hydroxylamine-

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containing compounds and their derivatives, which clearly embraces primary N-hydroxyl amines due to the fact that the reaction between the unwanted reactive oxygen species, is with the N-hydroxylamine-containing moiety.

In addition, the printed matter on a label or package insert of a kit or container does not lend patentable weight as a limitation of the claimed product, composition, or article of manufacture, absent a functional relationship between the label or package insert of a kit and the product, composition, or article of manufacture of a kit or container.

See *In re Haller* 73 USPQ 403 (CCPA 1947), where it is held that application of printed matter to old article cannot render the article patentable. In the opinion text of *In re Haller*, it is stated that: Whether the statement of intended use appears merely in the claim or in label on the product is immaterial so far as the question of Patentability is concerned. . . In accordance with the patent statutes, an article or composition of matter, in order to be patentable, must not only be useful and involve invention, but must also be new. If there is no novelty in an article or composition itself, then a patent cannot be properly granted on the article or composition, regardless of the use for which it is intended. The difficulty is not that there can never be invention in discovering a new process involving the use of an old article, but that the statutes make no provision for patenting of an article or composition which is not, in and of itself, new.

Also see *In re Venezia* 189 USPQ 49 (CCPA 1976), where kits are drawn to the structural attributes of interrelated component parts and not to activities that may or may not occur. Further, *In re Miller* 164 USPQ 46 (CCPA 1969) and *In re Gulak* (CAFC) 217

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USPQ 401 relate to a mathematical device and to a measuring cup respectively. In each of these cases, the printed matter is considered a patentable distinction because the function of the device depends upon the printed matter itself, which is a patentable distinction because the function of the device depends upon the printed matter itself, which is a part of the substrate; without the printed indicia or numbers, the substrates lose their function. Such is not the case with the instantly claimed articles or kits. The claimed articles of the kit remain fully functional absent the labeling or printed instructions for use.

Thus the instructions for use included in a kit or article manufacture constitute an "intended use" for that kit or article of manufacture. Intended use does not impart patentable weight to a product. See MPEP 2111.03: Intended use recitations and other types of functional language cannot be entirely disregarded. However, in apparatus, article and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. *In re Casey*, 370 F.2d 576, 152 USPQ 235 (CCPA 1967); *In re Otto*, 312 F.2d 937, 938, 136 USPQ 458, 459 (CCPA 1963) as well as *In re Ngai*, 70 USPQ2d 1862 (CAFC 2004).

In the instant case, the kit claims are drawn to an old article or composition, which further comprises labeling instructions. The intended use, which is recited on the label or package of the insert, lacks a function relationship because the insert or label

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does not physically or chemically affect the chemical nature within the article of manufacture, and furthermore, the old article or old composition of the kit can still be used by the skilled artisan for other purposes. Therefore the old article or composition which are comprised with the claimed kit are unpatentable over the prior art, because they function equally effectively with or without the labeling, and accordingly no functional relationship exists between the instructions for use and the composition.

Thus the claims are addressed as being drawn to an article of manufacture comprising an old composition of a kit and a package insert, the instructions on the insert bearing no patentable weight with regard to double patenting, 102 and 103 rejections.

Obviousness-type Double Patenting

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 1-57 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-58 of U.S. Patent No. 6,455,589. Although the conflicting claims are not identical, they are not patentably

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distinct from each other because both the instant invention and U.S. Patent No.

6,455,589 teach of compositions and methods of primary N-hydroxylamine compounds and pharmaceutically acceptable salts thereof with the intended use of reducing oxidative damage or delaying senescence.

16. Claims 1-57 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-58 of copending Application No. 10/722,820. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant invention and copending Application No. 10/722,820 teach of compositions and methods of primary N-hydroxylamine compounds and pharmaceutically acceptable salts thereof with the intended use of reducing oxidative damage or delaying senescence.

17. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. C. Jones whose telephone number is (571) 272-0578. The examiner can normally be reached on Mondays, Tuesdays, Thursday, and Fridays from 8:30 am to 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, may be reached at (571) 272-0951. The official fax No. for correspondence is (703) 872-9306.

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Also, please note that U.S. patents and U.S. patent application publications are no longer supplied with Office actions. Accordingly, the cited U.S. patents and patent application publications are available for download via the Office's PAIR, see <http://pair-direct.uspto.gov>. As an alternate source, all U.S. patents and patent application publications are available on the USPTO web site (www.uspto.gov), from the Office of Public Records and from commercial sources.

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DWAYNE JONES
PRIMARY EXAMINER

Tech. Ctr. 1614
September 19, 2004